Neurophysiological Effects of Temperature on the Mammalian Spinal Central Pattern Generator (CPG) Network for Locomotion

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Temperature sensation allows mammals to avoid tissue damage from extreme heat or cold conditions and to monitor fever and inflammatory responses to infection or injury. While dysregulation of temperature sensation has contributed to declines in human health (prolonged fevers, hypothermia, inflammation, etc.), the causes and specific mechanisms responsible for this dysregulation and the direct effects of temperature on the mammalian spinal cord are relatively unknown (Khan et al., 2007; Savage et al., 2016). Temperature-induced reflex pathways are initiated by primary sensory neurons located within the dorsal root ganglia (DRG) that synapse onto interneurons which in turn can activate motor neurons (Solinski & Hoon, 2019). Vanilloid transient receptor potential (TRPV) channels are a well-established family of receptors located throughout the nervous system that activate in response to a temperature range; specifically, TRPV4 is known to activate in response to non-noxious, warm temperatures (above 30°C) (Alessandri-Haber et al., 2003; Suzuki et al., 2003). To study the effects of temperature on mammalian central pattern generator (CPG) networks, spinal cords from postnatal (P) mice one to three days old (P1 – P3) were dissected via ventral laminectomy. The spinal cord preparations used either lacked sensory input by cutting all dorsal roots or contained semi-intact sensory inputs via DRG preservation. Extracellular ventral root recordings were obtained from lumbar L2 (flexor-related activity) and L5 (extensor-related activity) ventral roots. Once alternating bursting from motor neurons was achieved, the solution within the recording chamber was heated to 24°C using a temperature control system, and the temperature increased by 2°C increments every 10 minutes until the locomotor rhythm was completely disrupted and bursting was eradicated. To determine if the differences between DRG and non-DRG preparations were due to TRPV4 activation, a TRPV4 antagonist HC 067047 was applied to DRG-containing preparations.

The present study determined that the maintenance of DRGs affected burst amplitude while CPG activity via burst duration and cycle period generally resembled recordings from non-DRG preparations. Previous studies have found that increasing temperature reduces action potential durations in individual neurons due to alterations in ion channel diffusion rates, speed of conformational changes required to activate or inactivate channels, and rate of biochemical reactions responsible for inserting and removing channels from the cell membrane (Buzatu, 2009); therefore, increasing temperature may be manipulating the relationship between interneuron membrane potentials and the Nernst equilibirum potentials. Meanwhile, maintenance of DRG projections onto the lumbar CPG network may manipulate neuron recruitment by either a) altering the sensitivity of postsynaptic interneurons and motor neurons to serotonin (Crick & Wallis, 1991) or b) increasing glutamate release onto the CPG network, triggering glutamate-induced excitotoxicity and activation of inflammatory pathways (Fawley et al., 2015; Wang et al., 2019).

Upon the application of the TRPV4 antagonist to DRG preparations, the drug appeared to have minimal effects on CPG activity and further reduced burst amplitude as temperature increased. This may be due to a disuption in the glutamatergic pathway induced by typical TRPV4 activation, which would lead to an earlier crash temperature and reduced burst amplitudes (Li et al., 2013; Shibasaki et al., 2007). Additionally, developmental stage of the spinal cord rather than DRG preservation appeared to contribute to crash temperature differences. Previous studies have found that both the DRG and lumbar CPG of mice are highly neuroplastic during the first few weeks of development, which may suggest that the younger mice have more neurons present and/or less differentiated neurons that can withstand prolonged excitation (Chen et al., 2004; Namaka et al., 2001). Overall, the lumbar CPG neural network presents with a complex response to temperature that should be further evaluated to confirm the preliminary findings presented.

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